Supplementary Material (ESI) for Chemical Communications


# Supporting Information

## First Total Syntheses of (-)-Macrosphelides J, K and Elucidation of Their Absolute Configuration

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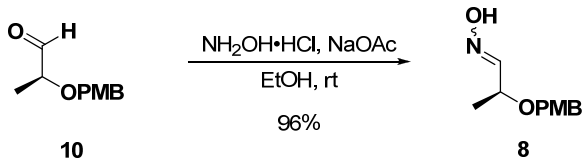
Total pages of supporting informations : (25).

## General Experimental

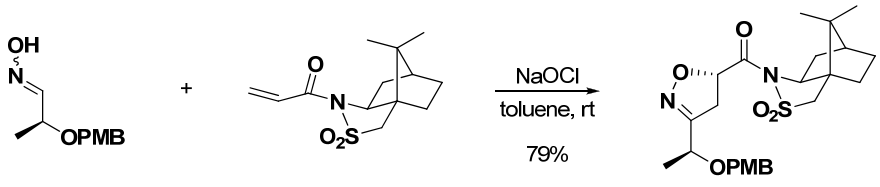
Unless noted otherwise, all starting materials and reagents were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran and $Et_2O$ were distilled from sodium benzophenone ketyl. Dichloromethane, chloroform, triethylamine, acetonitrile and pyridine were freshly distilled from calcium hydride. All solvents used for routine isolation of products and chromatography were reagent grade and glass distilled. Reaction flasks were dried at 100 °C. Air and moisture sensitive reactions were performed under argon atmosphere. Flash column chromatography was performed using silica gel 60 (230-400 mesh, Merck) with the indicated solvents. Thin-layer chromatography was performed using 0.25 mm silica gel plates (Merck). Optical rotations were measured with JASCO DIP-1000 digital polarimeter at ambient temperature using 100 nm cell of 2 mL capacity. Infrared spectra were recorded on a Perkin-Elmer 1710 FT-IR spectrometer. Mass spectra were obtained with VG Trio-2 GC-MS instrument. High resolution mass spectra were obtained with JEOL JMS-AX 505WA instrument. $^1H$ and $^{13}C$ NMR spectra were recorded on either a JEOL JNM-GCX 400 or JEOL JNM-LA 300 spectrometer as solutions in deuteriochloroform ($CDCl_3$). Chemical shifts are expressed in parts per million (ppm, $\delta$) downfield from tetramethylsilane and are referenced to the deuterated solvent ($CHCl_3$). $^1H$-NMR data were reported in the order of chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and/or multiple resonance), number of protons, and coupling constant in hertz (Hz).




10 8

**Aldoxime (8)**

To a solution of aldehyde **10** (6.11 g, 31.5 mmol) in EtOH (50 mL) were added NaOAc (6.20 g, 75.6 mmol) and $NH_2OH$•HCl (2.63 g, 37.8 mmol) subsequently at ambient temperature. After the reaction mixture was vigorously stirred for 3 h at the same temperature, the mixture was concentrated under reduced pressure. Brine was added to the residue and then extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 4) to afford 6.30 g (96%) of aldoxime **8** as a white solid: FT-IR (thin film, neat) $\nu_{max}$ 3334, 2934, 1612, 1586, 1514, 1464, 1373, 1303 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 7.96 (s, 1H), 7.33(d, 1H, *J* = 7.5 Hz), 7.24 (d, 2H, *J* = 8.3 Hz), 6.86 (d, 2H, *J* = 8.6 Hz), 4.43 (m, 2H), 4.07 (m, 1H), 3.78 (s, 3H), 1.33 (d, 3H, *J* = 6.6 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 159.3, 155.3, 129.9, 129.5, 129.5, 113.8, 113.8, 71.7, 70.3, 55.3, 19.4; LR-MS (FAB+) *m/z* 210 (M+H).

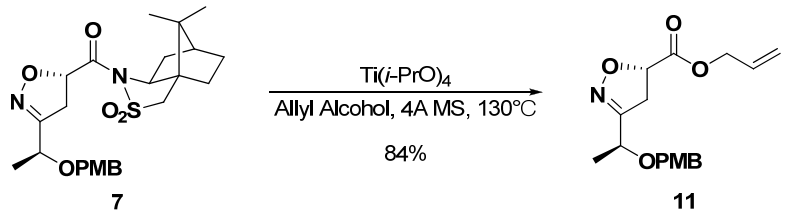



8 9 **7** (d.r. > 10 : 1)

**Isoxazoline (7)**

To a solution of aldoxime **8** (772 mg, 3.69 mmol) and acrylate **9** (663 mg, 2.46 mmol) in toluene (50 mL) were added aqueous NaOCl (2.93 mL, 4.92 mmol, c.a. 10%) at ambient temperature. The reaction mixture was stirred for 1 h at the same temperature and diluted with $H_2O$. The aqueous layer was extracted with EtOAc and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was

purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 2) to afford 922 mg (79 %) of isoxazoline **7** as a pale yellow foamy solid: $[\alpha]_D^{20}$ +144 (*c* 2.34, $CHCl_3$); FT-IR (thin film, neat) $\nu_{max}$ 2959, 1698, 1613, 1514, 1460, 1392, 1335 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 7.27 (d, 2H, *J* = 8.4 Hz), 6.86 (d, 2H, *J* = 8.6 Hz), 5.55 (dd, 1H, *J* = 10.8, 6.4 Hz), 4.44 (q, 1H, *J* = 6.6 Hz), 4.38 (m, 2H), 3.91 (dd, 1H, *J* = 7.9, 5.0 Hz), 3.78 (s, 3H), 3.48 (m, 2H), 3.34 (m, 2H), 2.14 (m, 1H), 2.07 (m, 2H), 1.89 (m, 2H), 1.40 (m, 2H), 1.36 (d, 3H, *J* = 6.6 Hz), 1.18 (s, 3H), 0.97 (s, 3H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) δ 168.5, 159.5, 159.3, 129.8, 129.8, 129.6, 113.8, 113.8, 76.8, 70.3, 68.8, 65.2, 55.2, 52.9, 49.0, 47.8, 44.6, 38.1, 37.0, 32.8, 26.4, 20.9, 19.8, 19.0; LR-MS (FAB+) *m/z* 477 (M+H); HR-MS (FAB+) calcd for $C_{24}H_{33}N_2O_6S$ (M+H) 477.2059; found 477.2057.

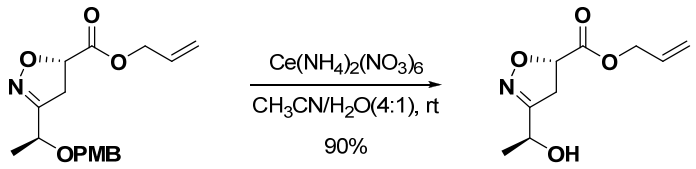



7 11

**Allyl ester (11)**

To a solution of isoxazoline **7** (902 mg, 1.89 mmol) in the presence of 4 Å molecular sieves (473 mg, 250 mg/mmol) in allyl alcohol (50 mL, 0.0379 M), was added Ti(O*i*-Pr)$_4$ (1.66 mL, 5.67 mmol) at 130 ℃. After the reaction mixture was vigorously stirred for 1 h at same temperature, the mixture was quenched with saturated aqueous $NH_4Cl$, and then extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 3) to afford 508 mg (84%) of allyl ester **11** as a yellow oil: $[\alpha]_D^{20}$ +17.2 (*c* 2.18, $CHCl_3$); FT-IR (thin film, neat) $\nu_{max}$ 2938, 1743, 1613, 1514, 1458, 1375 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 7.23 (d, 2H, *J* = 8.8 Hz), 6.85 (d, 2H, *J* = 8.8 Hz), 5.90 (m, 1H), 5.37 - 5.22 (m, 2H), 5.04 (t, 1H, *J* = 8.7 Hz), 4.66 (dt, 2H, *J* = 5.9, 1.3 Hz), 4.45 (q, 1H, *J* = 6.6 Hz), 4.35 (m, 2H), 3.78 (s, 3H), 3.29 (d, 2H, *J* =

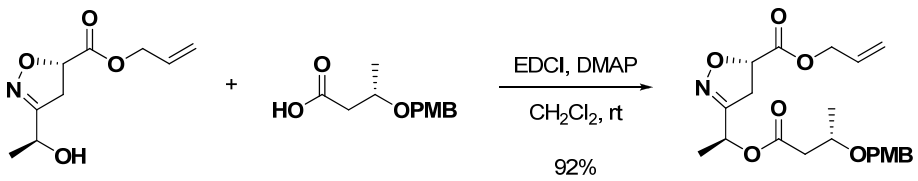
8.6 Hz), 1.36 (d, 3H, *J* = 6.6 Hz) ; $^{13}$C-NMR ($CDCl_3$, 100 MHz) δ 169.8, 159.5, 159.3, 131.2, 129.6, 129.6, 129.4, 119.2, 113.8, 113.8, 77.1, 70.4, 68.9, 66.2, 55.2, 36.9, 18.9 ; LR-MS (FAB+) *m/z* 320 (M+H); HR-MS (FAB+) calcd for $C_{17}H_{22}NO_5$ (M+H) 320.1498; found 320.1502.




**11** **12**

**PMB Deprotected alcohol (12)**

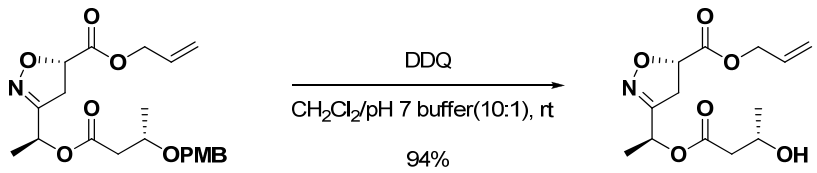
To a solution of allyl ester **11** (637 mg, 2.00 mmol) in $CH_3CN$ (80 mL) and $H_2O$ (20 mL) at ambient temperature was added ammonium cerium(Ⅳ) nitrate (3.29 g, 6.00 mmol). After stirring for 3 h at the same temperature, the reaction mixture was quenched with $H_2O$. The aqueous layer was extracted with EtOAc and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 1) to afford 356 mg (90%) of PMB deprotected alcohol **12** as a pale yellow oil: $[\alpha]_D^{20}$ +128 (*c* 0.653, $CHCl_3$); FT-IR (thin film, neat) $\nu_{max}$ 3432, 2982, 1744, 1647, 1439, 1376 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 5.91 (m, 1H), 5.37 - 5.25 (m, 2H), 5.05 (dd, 1H, *J* = 9.9, 8.3 Hz), 4.71 (m, 1H), 4.67 (dt, 2H, *J* = 5.9, 1.3 Hz), 3.33 (m, 2H), 2.13 (d, 1H, *J* = 4.2 Hz), 1.43 (d, 3H, *J* = 6.6); $^{13}$C-NMR ($CDCl_3$, 100 MHz) δ 170.0, 161.2, 131.1, 119.4, 77.4, 66.4, 63.5, 37.6, 20.7; LR-MS (FAB+) *m/z* 200 (M+H); HR-MS (FAB+) calcd for $C_9H_{14}NO_4$ (M+H) 200.0923; found 200.0924.




**12** **6** **13**

**PMB Protected β-hydroxy ester (13)**

To a solution of acid **6** (529 mg, 2.36 mmol) and alcohol **12** (312 mg, 1.57 mmol) in $CH_2Cl_2$ (50 mL) at ambient temperature were added EDCI (602 mg, 3.14 mmol), DMAP (383 mg, 3.14 mmol). After stirring for 2 h at the same temperature, the reaction mixture was quenched with $H_2O$. The aqueous layer was extracted with $CH_2Cl_2$ and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 3) to afford 584 mg (92%) of ester **13** as a yellow oil: $[\alpha]_D^{20}$ +49.6 (*c* 1.01, $CHCl_3$); FT-IR (thin film, neat) $\nu_{max}$ 2937, 1742, 1613, 1514, 1451, 1376 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 7.20 (d, 2H, *J* = 8.4 Hz), 6.84 (d, 2H, *J* = 8.6 Hz), 5.90 (m, 1H), 5.67 (q, 1H, *J* = 6.6 Hz), 5.36 – 5.24 (m, 2H), 4.88 (dd, 1H, *J* = 11.0, 7.5 Hz), 4.64 (dt, 2H, *J* = 5.9, 1.3 Hz), 4.43 (m, 2H), 3.99 (m, 1H), 3.77 (s, 3H), 3.15 (m, 2H), 2.52 (m, 2H), 1.48 (d, 3H, *J* = 6.6 Hz), 1.25 (d, 3H, *J* = 6.2 Hz); $^{13}$C-NMR ($CDCl_3$, 100 MHz) δ 170.4, 169.4, 159.2, 157.7, 131.2, 130.3, 129.3, 129.3, 119.2, 113.7, 113.7, 77.7, 71.7, 70.5, 66.3, 65.4, 55.2, 42.1, 38.6, 19.6, 17.6; LR-MS (FAB+) *m/z* 406 (M+H); HR-MS (FAB+) calcd for $C_{21}H_{28}NO_7$ (M+H) 406.1866; found 406.1872.

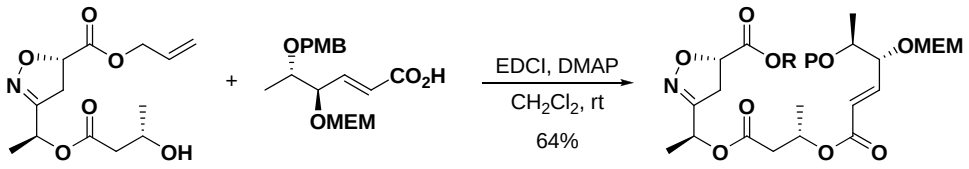



**13** **5**

**β-hydroxy ester (5)**

To a solution of PMB ether **13** (379 mg, 0.935 mmol) in $CH_2Cl_2$ (30 mL) and phosphate buffer solution (3 mL, pH 7.0) at ambient temperature was added DDQ (638 mg, 2.81 mmol). The reaction mixture was stirred for 3 h and the reaction mixture was diluted with $CH_2Cl_2$, filtered under reduced pressure. The organic layer was washed with $H_2O$ and aqueous layer was extracted with $CH_2Cl_2$. The organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column

chromatography on silica gel (EtOAc : *n*-hexane = 1 : 1) to afford 250 mg (94%) of alcohol **5** as a yellow oil: $[\alpha]_D^{20}$ +90.4 (*c* 1.51, $CHCl_3$); FT-IR (thin film, neat) $\nu_{max}$ 3540, 3087, 2978, 1740, 1644, 1452, 1377 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 5.82 (m, 1H), 5.61 (q, 1H, *J* = 6.5 Hz), 5.28 - 5.15 (m, 2H), 4.97 (dd, 1H, *J* = 11.0, 6.9 Hz), 4.57 (d, 2H, 5.9), 4.11 (m, 1H), 3.21 (m, 2H), 3.06 (s, 1H), 2.39 (m, 2H), 1.42 (d, 3H, *J* = 6.8 Hz), 1.14 (d, 3H, *J* = 6.2); $^{13}$C-NMR ($CDCl_3$, 100 MHz) δ 171.3, 169.3, 157.6, 131.0, 119.0, 77.5, 66.1, 65.5, 64.2, 43.0, 38.1, 22.5, 17.6; LR-MS (FAB+) *m/z* 286 (M+H); HR-MS (FAB+) calcd for $C_{13}H_{20}NO_6$ (M+H) 286.1291; found 286.1300.

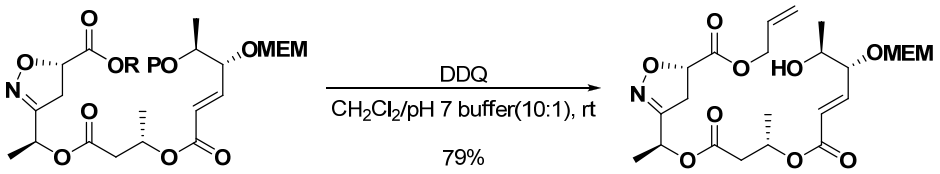



**5** **4** **14** (R= Allyl, P= PMB)

**MEM Protected γ-hydroxy α,β-unsaturated ester (14)**

To a solution of acid **4** (655 mg, 1.85 mmol) and alcohol **5** (376 mg, 1.32 mmol) in $CH_2Cl_2$ (40 mL) at ambient temperature were added EDCI (506 mg, 2.64 mmol), DMAP (322 mg, 2.64 mmol). After stirring for 3 h at the same temperature, the reaction mixture was quenched with $H_2O$. The aqueous layer was extracted with $CH_2Cl_2$ and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 1) to afford 523 mg (64%) of ester **14** as a yellow oil: $[\alpha]_D^{20}$ +25.2 (*c* 1.74, $CHCl_3$); FT-IR (thin film, neat) $\nu_{max}$ 2937, 1743, 1656, 1613, 1514, 1453, 1377 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 7.18 (d, 2H, *J* = 8.6 Hz), 6.81 (m, 1H), 6.80 (d, 2H, *J* = 8.6 Hz), 5.95 (dd, 1H, *J* = 15.8, 1.5 Hz), 5.86 (m, 1H), 5.61 (q, 1H, *J* = 6.6 Hz), 5.32 - 5.20 (m, 2H), 5.28 (m, 1H), 4.98 (dd, 1H, *J* = 10.6, 7.7 Hz), 4.68 (m, 2H), 4.61 (dt, 2H, *J* = 5.9, 1.3 Hz), 4.45 (s, 2H), 4.27 (m, 1H), 3.74 (s, 3H), 3.72 (m, 1H), 3.57 (m, 2H), 3.44 (m, 2H), 3.30 (s, 3H), 3.19 (m, 2H), 2.59 (m, 2H), 1.41 (d, 3H, *J* = 6.6 Hz), 1.28 (d, 3H, *J* = 6.2 Hz), 1.11 (d, 3H, *J* = 6.2 Hz); $^{13}$C-NMR ($CDCl_3$, 100 MHz) δ 169.3, 168.9, 165.0,

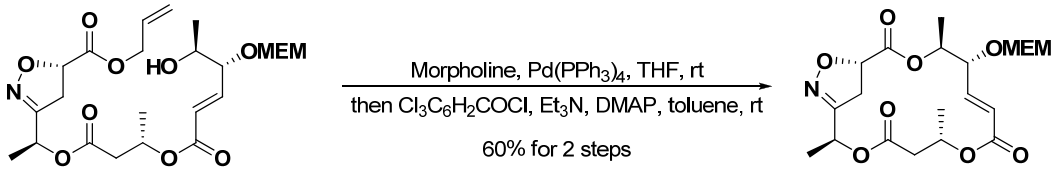
159.0, 157.3, 145.6, 131.1, 130.3, 129.1, 129.1, 122.9, 119.1, 113.6, 113.6, 93.9, 92.4, 92.2, 77.6, 76.7, 71.5, 70.7, 67.1, 66.2, 65.7, 58.9, 55.2, 40.7, 38.3, 19.8, 17.7,15.5; LR-MS (FAB+) *m/z* 622 (M+H); HR-MS (FAB+) calcd for $C_{31}H_{44}NO_{12}$ (M+H) 622.2864; found 622.2871.




**14** (R= Allyl, P= PMB) **15**

**PMB Deprotected secondary alcohol (15)**

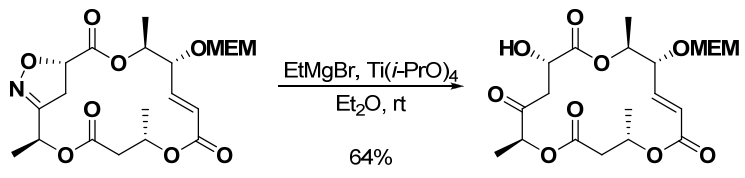
To a solution of PMB ether **14** (523 mg, 0.842 mmol) in $CH_2Cl_2$ (50 mL) and phosphate buffer solution (5 mL, pH 7.0) at ambient temperature was added DDQ (574 mg, 2.52 mmol). The reaction mixture was stirred for 2 h and the reaction mixture was diluted with $CH_2Cl_2$, filtered under reduced pressure. The organic layer was washed with $H_2O$ and aqueous layer was extracted with $CH_2Cl_2$. The organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 3 : 2) to afford 332 mg (79%) of alcohol **15** as a yellow oil: $[\alpha]_D^{20}$ +19.0 (*c* 0.753, $CHCl_3$); FT-IR (thin film, neat) $\nu_{max}$ 3464, 2936, 1744, 1654, 1454, 1377 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 6.83 (dd, 1H, *J* = 15.7, 6.2 Hz), 5.99 (dd, 1H, *J* = 15.6, 1.4 Hz), 5.90 (m, 1H), 5.65 (q, 1H, *J* = 6.5 Hz), 5.36 – 5.24 (m, 2H), 5.32 (m, 1H), 5.04 (dd, 1H, *J* = 11.1, 7.4 Hz), 4.72 (m, 2H), 4.66 (dt, 2H, *J* = 5.9, 1.3 Hz), 4.19 (m, 1H) 3.92 (m, 1H), 3.74 (m, 2H), 3.53 (t, 2H, *J* = 4.5), 3.36 (s, 3H), 3.24 (m, 2H), 2.87 (d, 1H, *J* = 5.9), 2.62 (m, 2H), 1.46 (d, 3H, *J* = 6.6), 1.32 (d, 3H, *J* = 6.2 Hz), 1.12 (d, 3H, *J* = 6.6 Hz),); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 169.4, 168.9, 164.9, 157.3, 144.4, 131.2, 123.6, 119.1, 94.4, 80.8, 77.7, 71.6, 68.9, 67.5, 67.2, 66.3, 65.8, 58.9, 40.8, 38.4, 19.9, 19.8, 17.7; LR-MS (FAB+) *m/z* 524 (M+Na); HR-MS (FAB+) calcd for $C_{23}H_{35}NO_{11}Na$ (M+Na) 524.2108; found 524.2092.




15 3

**16-Membered macrolactone (3)**

To a solution of alcohol **15** (191 mg, 0.381 mmol) in THF (7 mL) at ambient temperature were added $Pd(PPh_3)_4$ (440 mg, 0.381 mmol) and morpholine (70.0 μL, 0.762 mmol). The mixture was stirred for 12 h at the same temperature and quenched with 1*N* HCl and extracted with EtOAc three times. The organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. This crude mixture was used for next step without further purification. To a solution of acid in toluene (10 mL) were added $Et_3N$ (1.59 mL, 11.4 mmol) and 2,4,6-trichlorobenzoyl chloride (1.19 mL, 7.62 mmol) at 0 $^oC$. The mixture was warmed to ambient temperature and stirred for 2 h before removing the THF under reduced pressure. The residue was redissolved in toluene (10 mL) and added slowly to a rapidly stirred solution of DMAP (1.86 g, 15.2 mmol) in toluene (90 mL). The mixture was stirred for 24 h and quenched with $H_2O$. The reaction mixture was extracted with EtOAc and the organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 2 : 1) to afford 102 mg (60%) of ester **3** as a pale yellow oil

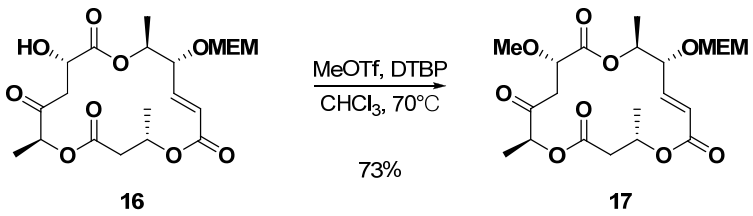



3 16

**β-Hydroxy ketone (16)**

To a solution of $Ti(O\textit{i}\text{-}Pr)_4$ (0.495 mL, 1.69 mmol) in $Et_2O$ (25 mL) was added EtMgBr (0.450 mL of 3.0 M solution in $Et_2O$, 1.35 mmol) at ambient temperature. The initially colorless solution turned black-brown and heterogeneous over the course of EtMgBr

addition. The reaction mixture was stirred for 2 h at the same temperature. To a solution of isoxazoline **3** (25.0 mg, 56.4 μmol) in $Et_2O$ (2 mL) was added the black-brown reagent at ambient temperature. After stirring for 3 h at the same temperature, quenched with $H_2O$, the reaction mixture was filtered with silica gel under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 2 : 1) to afford 16 mg (64%) of ester **16** as a pale yellow oil: $[\alpha]_D^{20}$ –73.7 (*c* 0.520, $CH_3OH$); FT-IR (thin film, neat) $\nu_{max}$ 3482, 2935, 1731, 1661, 1453, 1372 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 6.67 (dd, 1H, *J* = 15.8, 8.2 Hz), 5.98 (d, 1H, *J* = 15.8 Hz), 5.33 (m, 1H), 5.18 (q, 1H, *J* = 6.7 Hz), 4.94 (m, 1H), 4.68 (m, 2H), 4.55 (m, 1H), 4.07 (m, 1H), 3.68 (m, 2H), 3.52 (t, 2H, *J* = 4.6 Hz), 3.36 (s, 3H), 2.99 (s, 1H), 2.70 (m, 2H), 2.65 (m, 2H), 1.38 (d, 6H, *J* = 6.6 Hz), 1.35 (d, 3H, *J* = 6.4 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 204.2, 172.7, 169.9, 164.2, 144.9, 125.6, 93.7, 78.1, 75.9, 72.2, 71.6, 68.6, 67.5, 66.3, 59.0, 42.3, 41.4, 20.1, 17.7, 15.6; LR-MS (FAB+) *m/z* 447 (M+H); HR-MS (FAB+) calcd for $C_{20}H_{31}O_{11}$ (M+H) 447.1866; found 447.1860.

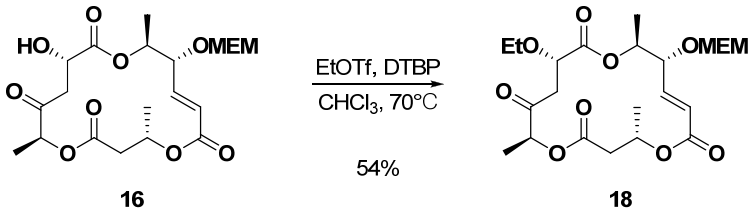



**16** **17**

**β-Methoxy ketone (17)**

To a solution of β-hydroxy ketone **16** (12 mg, 26.9 μmol) in $CHCl_3$ (1 mL) at ambient temperature were added 2,6-di-*t*-butylpyridine (0.181 mL, 0.807 mmol) and MeOTf (88.5 μL, 0.807 mmol). The mixture was warmed to 80℃ and stirred for 12 h. The mixture was quenched with saturated aqueous $NH_4Cl$, and then extracted with $CH_2Cl_2$. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 1) to afford 9 mg (73%) of allyl ester **17** as a colorless oil: FT-IR (thin film, neat) $\nu_{max}$ 2933, 1731, 1662, 1454, 1372 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 6.69 (dd, 1H, *J*

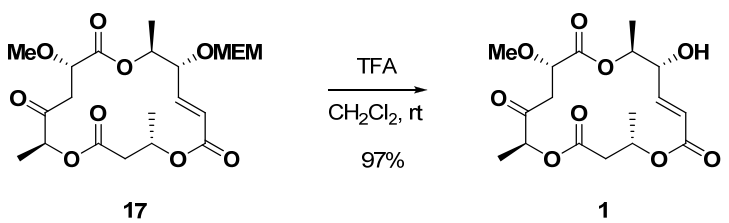
= 15.8, 8.2 Hz), 5.97 (d, 1H, *J* = 15.8 Hz), 5.30 (m, 1H), 5.19 (q, 1H, *J* = 6.7 Hz), 4.98 (m, 1H), 4.68 (m, 2H), 4.19 (dd, 1H, *J* = 9.0, 3.9 Hz), 4.05 (t, 1H, *J* = 8.5 Hz), 3.69 (m, 2H), 3.52 (t, 2H, *J* = 4.5 Hz), 3.36 (s, 3H), 3.36 (s, 3H), 2.67 (m, 2H), 2.66 (m, 2H), 1.37 (d, 6H, *J* = 6.2 Hz), 1.34 (d, 3H, *J* = 6.4 Hz); LR-MS (FAB+) *m/z* 483 (M+Na); HR-MS (FAB+) calcd for $C_{21}H_{32}O_{11}Na$ (M+Na) 483.1842; found 483.1822.




**16** **18**

**β-Ethoxy ketone (18)**

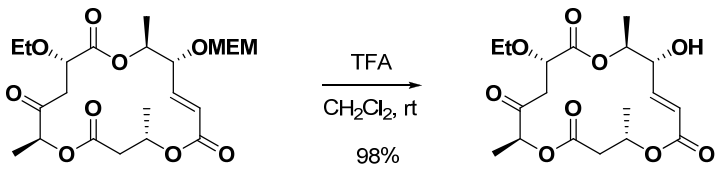
To a solution of β-hydroxy ketone **16** (14 mg, 31.4 μmol) in $CHCl_3$ (1 mL) at ambient temperature were added 2,6-di-*t*-butylpyridine (0.212 mL, 0.942 mmol) and EtOTf (0.122 mL, 0.942 mmol). The mixture was warmed to 80℃ and stirred for 12 h. The mixture was quenched with saturated aqueous $NH_4Cl$, and then extracted with $CH_2Cl_2$. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 1) to afford 8 mg (54%) of allyl ester **18** as a colorless oil: $^1$H-NMR ($CDCl_3$, 300 MHz) δ 6.69 (dd, 1H, *J* = 15.8, 8.1 Hz), 5.97 (d, 1H, *J* = 15.9 Hz), 5.29 (m, 1H), 5.20 (q, 1H, *J* = 6.7 Hz), 4.98 (m, 1H), 4.68 (m, 2H), 4.28 (dd, 1H, *J* = 9.2, 3.5 Hz), 4.05 (t, 1H, *J* = 8.6 Hz), 3.68 (m, 2H), 3.52 (t, 2H, *J* = 4.5 Hz), 3.52 (m, 2H), 3.36 (s, 3H), 2.68 (m, 2H), 2.66 (m, 2H), 1.37 (d, 3H, *J* = 6.8 Hz), 1.36 (d, 3H, *J* = 6.2 Hz), 1.34 (d, 3H, *J* = 6.4 Hz), 1.14 (t, 3H, *J* = 7.1 Hz); LR-MS (FAB+) *m/z* 497 (M+Na); HR-MS (FAB+) calcd for $C_{22}H_{34}O_{11}Na$ (M+Na) 497.1999; found 497.2018.




**17** **1**

**(-)-Macrosphelide J (1)**

To a solution of **17** (4.1 mg, 8.91 μmol) in $CH_2Cl_2$ (0.5 mL) was added trifluoroacetic acid (0.5 mL) at the ambient temperature. After stirring for 12 h, the reaction mixture was concentrated *in vacuo* and purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 1) to afford 3.2 mg (97%) of (-)-macrosphelide J **1** as a colorless oil: $[\alpha]_D^{20}$ –40.4 (*c* 0.100, $CH_3OH$), the natural **1** $[\alpha]_D^{20}$ –41 (*c* 0.200, $CH_3OH$); FT-IR (thin film, neat) $\nu_{max}$ 3478, 2929, 1730, 1454, 1374 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 6.79 (dd, 1H, *J* = 15.6, 4.2 Hz), 6.10 (dd, 1H, *J* = 15.8, 1.8 Hz), 5.43 (m, 1H), 5.20 (q, 1H, *J* = 6.8 Hz), 4.94 (m, 1H), 4.25 (dd, 1H, *J* = 9.4, 3.2 Hz), 4.22 (m, 1H), 3.38 (s, 3H), 2.72 (m, 2H), 2.69 (m, 2H), 1.43 (d, 3H, *J* = 6.6 Hz), 1.38 (d, 3H, *J* = 6.8 Hz), 1.35 (d, 3H, *J* = 6.4 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 202.7, 172.9, 169.8, 164.2, 144.2, 123.3, 76.6, 75.4, 74.7, 74.6, 68.5, 58.8, 42.0, 41.0, 20.0, 18.2, 15.0; LR-MS (FAB+) *m/z* 395 (M+Na); HR-MS (FAB+) calcd for $C_{17}H_{24}O_9Na$ (M+Na) 395.1318; found 395.1308.

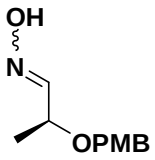



**18** **2**

**(-)-Macrosphelide K (2)**

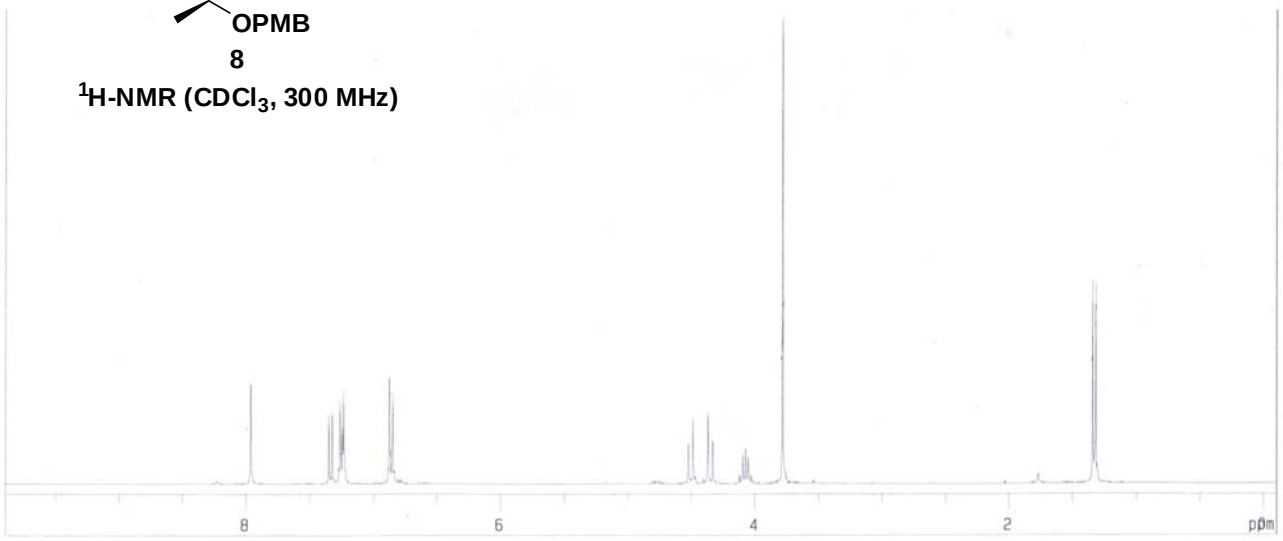
To a solution of **18** (4.0 mg, 8.44 μmol) in $CH_2Cl_2$ (0.5 mL) was added trifluoroacetic acid (0.5 mL) at the ambient temperature. After stirring for 12 h, the reaction mixture was concentrated *in vacuo* and purified by flash column chromatography on silica gel (EtOAc : *n*-hexane = 1 : 1) to afford 3.2 mg (98%) of (-)-macrosphelide K **2** as a colorless oil: $[\alpha]_D^{20}$ –55.8 (*c* 0.167, $CH_3OH$), the natural **2** $[\alpha]_D^{20}$ –59 (*c* 0.200, $CH_3OH$); FT-IR (thin film, neat) $\nu_{max}$ 3396, 2924, 2853, 1736, 1540, 1459, 1374 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) δ 6.79 (dd, 1H, *J* = 15.9, 4.0 Hz), 6.11 (dd, 1H, *J* = 15.6, 1.4 Hz), 5.42 (m, 1H), 5.21 (q, 1H, *J* = 6.7 Hz), 4.93 (m, 1H), 4.34 (dd, 1H, *J* = 9.1, 3.4 Hz),

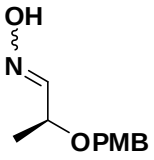
4.20 (m, 1H), 3.53 (m, 2H), 2.72 (m, 2H), 2.70 (m, 2H), 1.42 (d, 3H, $J$ = 6.8 Hz), 1.38 (d, 3H, $J$ = 6.6 Hz), 1.35 (d, 3H, $J$ = 6.2 Hz), 1.15 (t, 3H, $J$ = 6.9 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) δ 202.7, 173.3, 169.7, 164.2, 144.2, 123.3, 76.6, 75.4, 74.8, 73.0, 68.5, 66.9, 42.1, 41.0, 19.9, 18.2, 15.0, 15.0; LR-MS (FAB+) *m/z* 409 (M+Na); HR-MS (FAB+) calcd for $C_{18}H_{26}O_9Na$ (M+Na) 409.1475; found 409.1462.




**8**

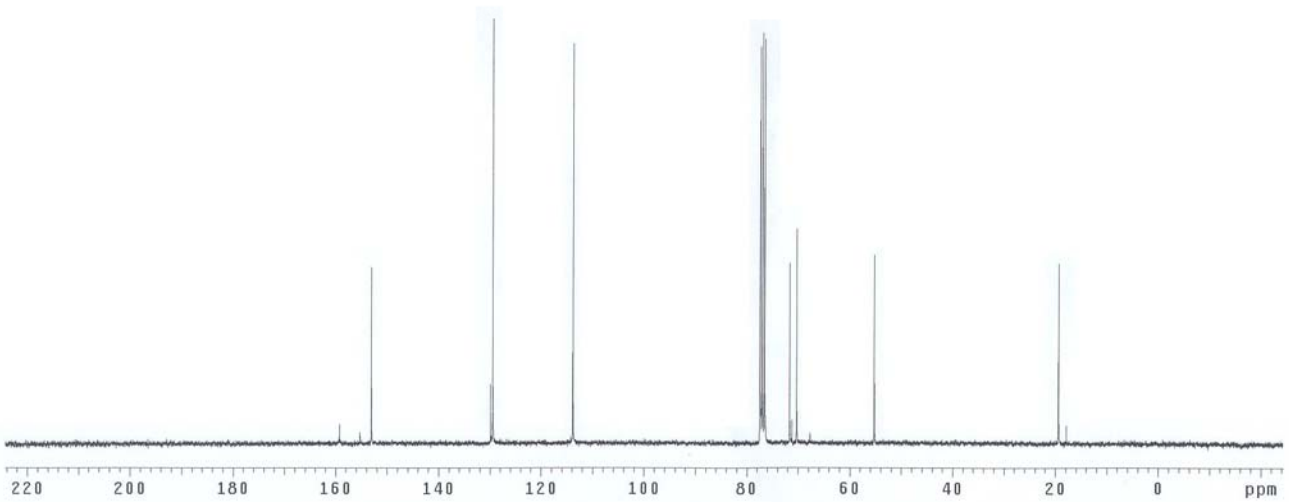
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**

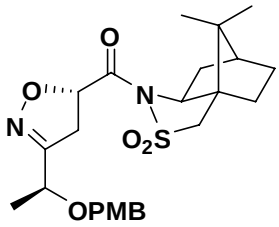



**8**

**$^{13}$C-NMR ($CDCl_3$, 75 MHz)**

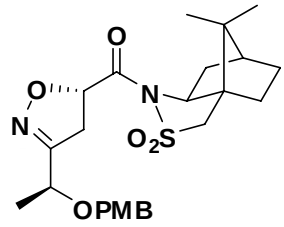





**7**

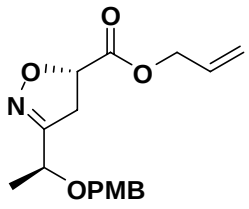
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**




**7**

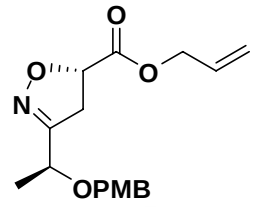
**$^{13}$C-NMR ($CDCl_3$, 100 MHz)**




**11**

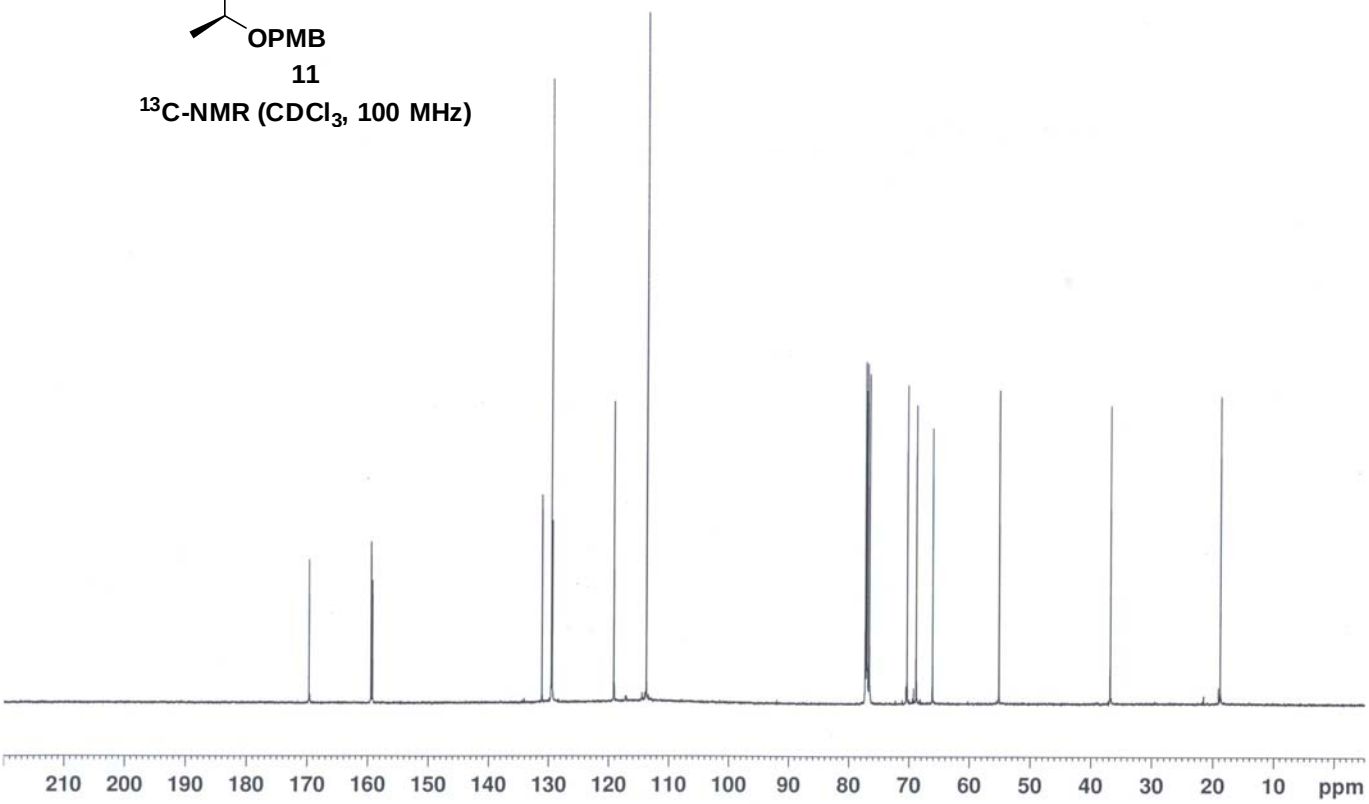
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**

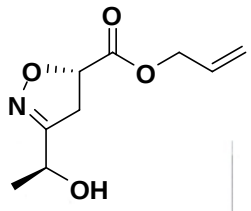



**11**

**$^{13}$C-NMR ($CDCl_3$, 100 MHz)**

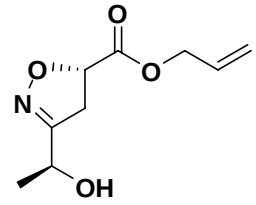




**12**

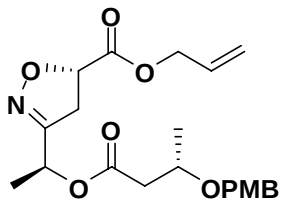
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**



**12**

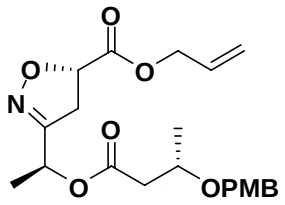
**$^{13}$C-NMR ($CDCl_3$, 100 MHz)**




**13**

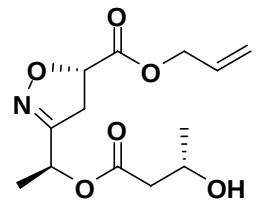
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**



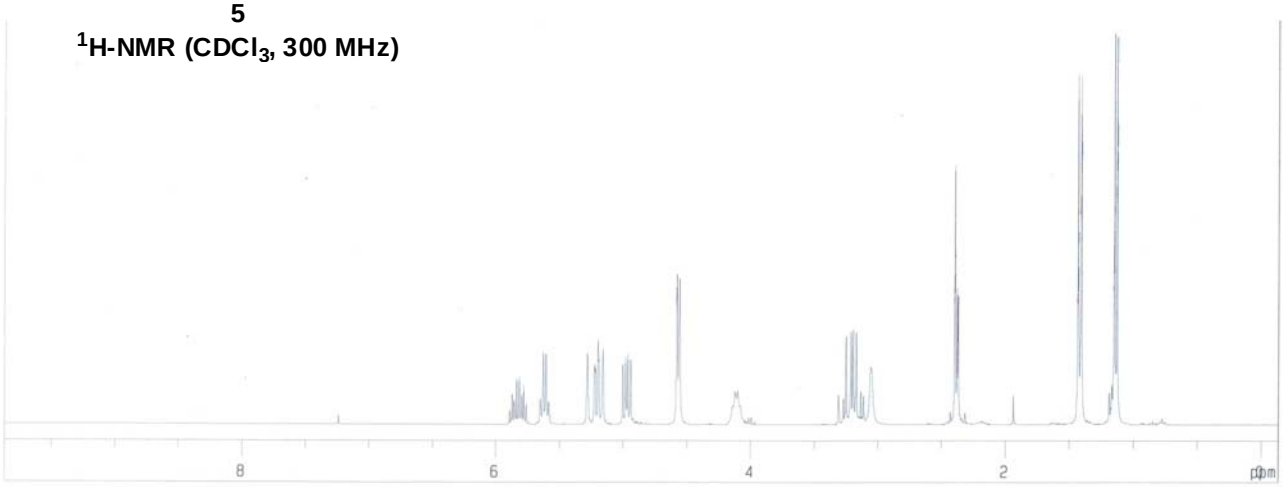

**13**

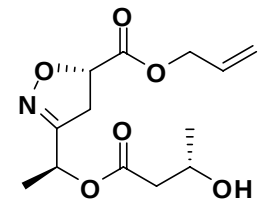
**$^{13}$C-NMR ($CDCl_3$, 100 MHz)**



**5**

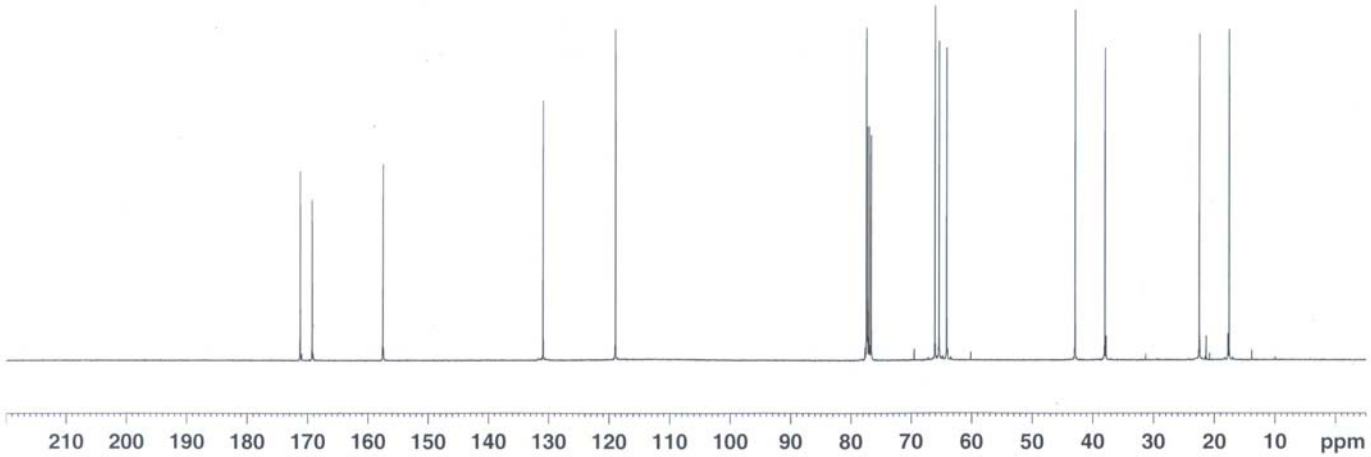
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**

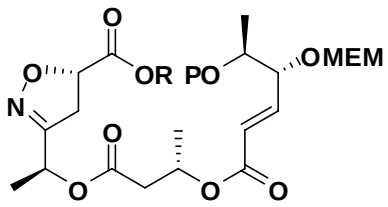


**5**

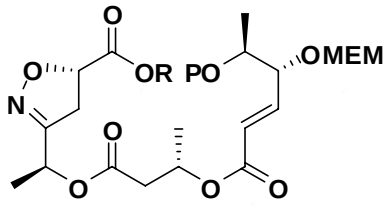
**$^{13}$C-NMR ($CDCl_3$, 100 MHz)**



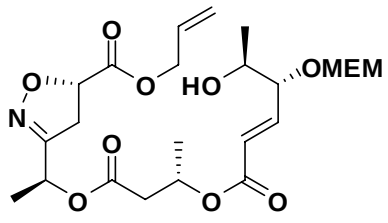



**14 (R= Allyl, P= PMB)**
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**



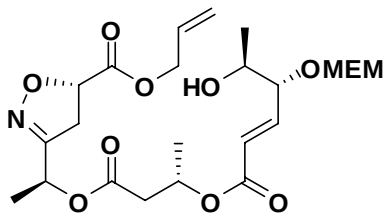

**14 (R= Allyl, P= PMB)**
**$^{13}$C-NMR ($CDCl_3$, 100 MHz)**




**15**

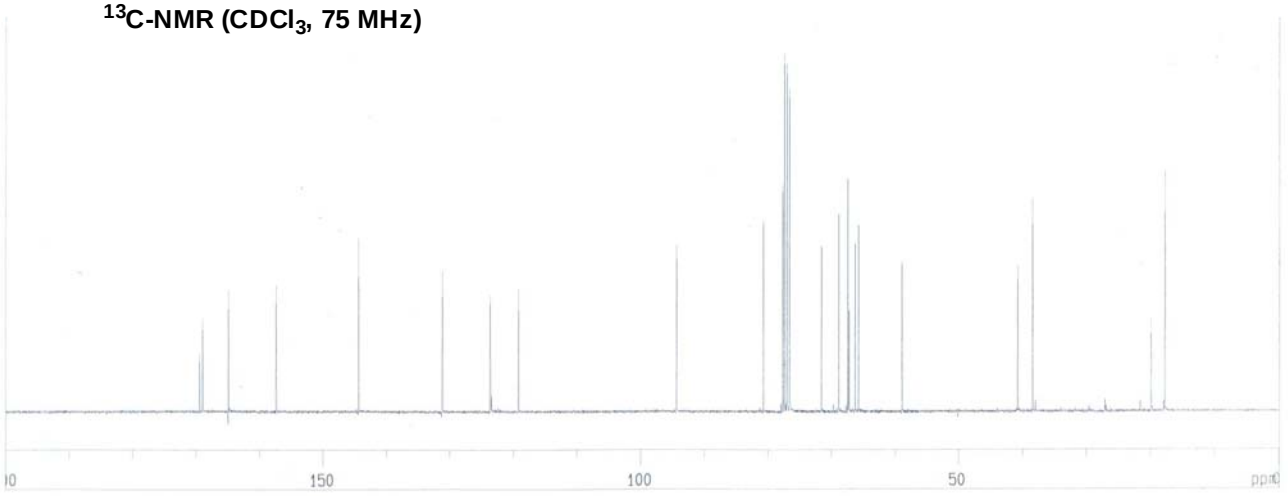
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**

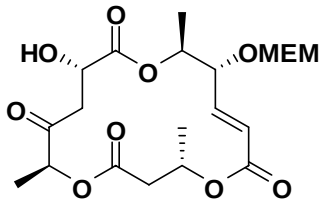



**15**

**$^{13}$C-NMR ($CDCl_3$, 75 MHz)**

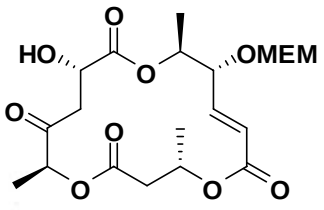





**16**

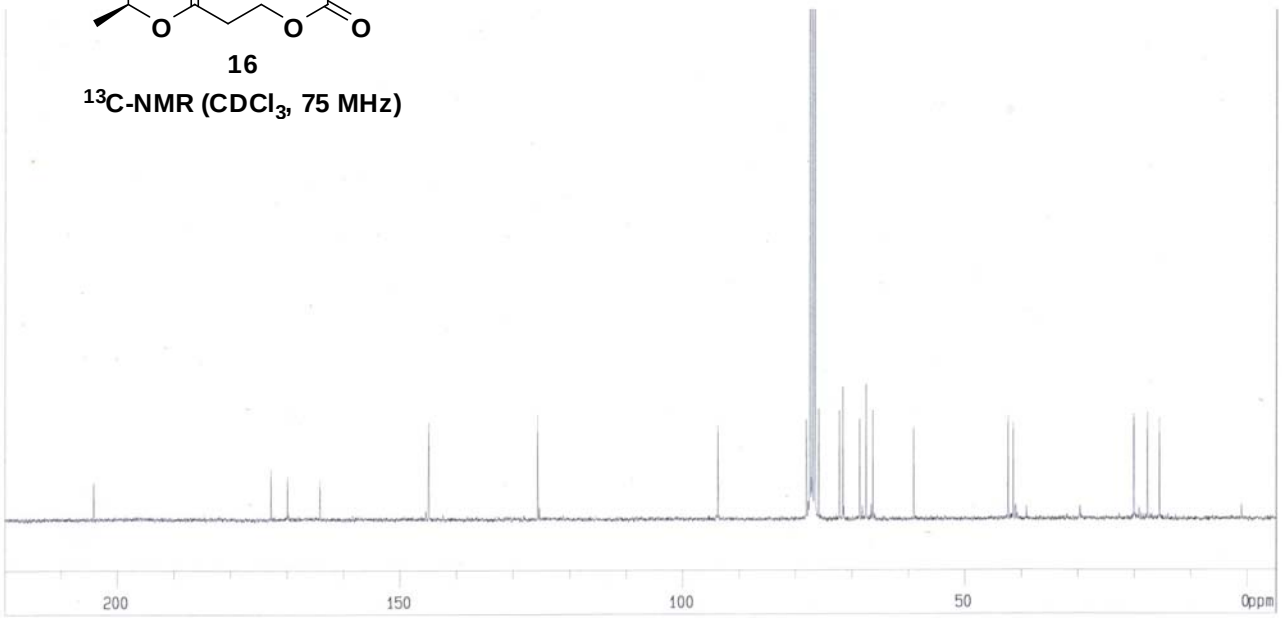
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**

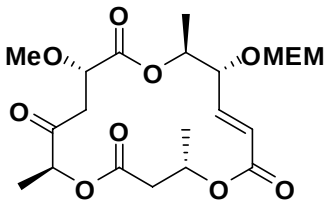



**16**

**$^{13}$C-NMR ($CDCl_3$, 75 MHz)**

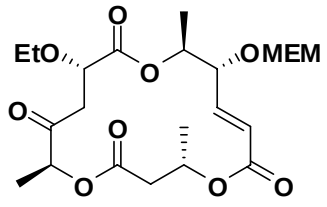





**17**

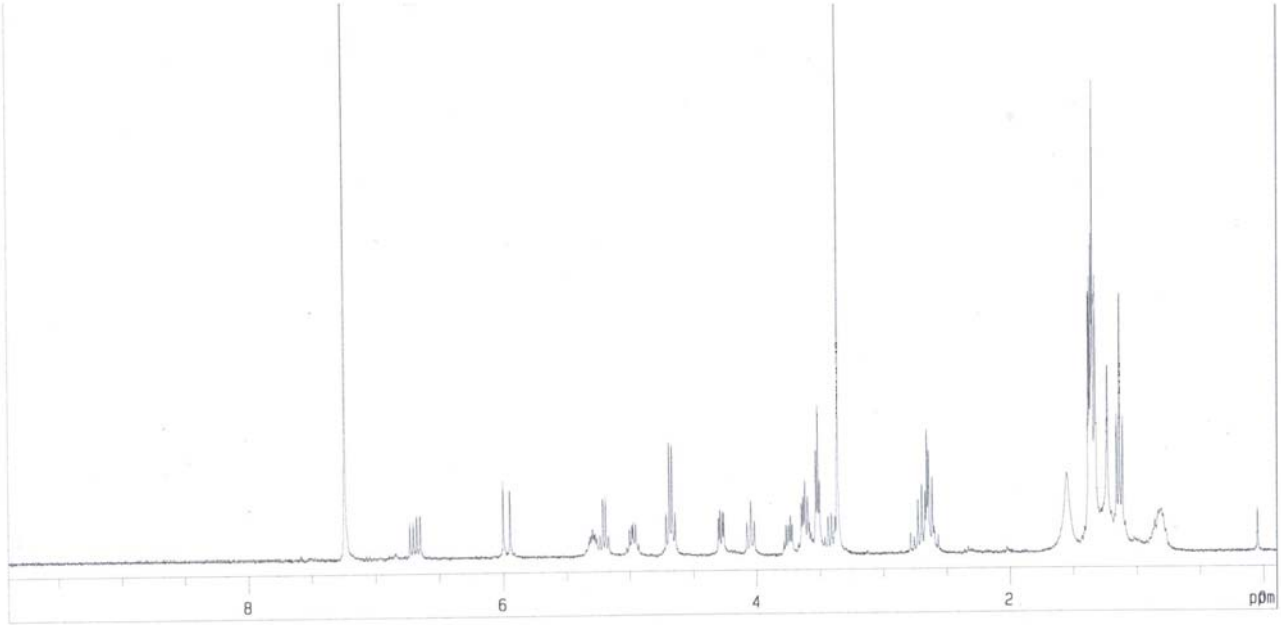
**$^1$H-NMR ($CDCl_3$, 300 MHz)**

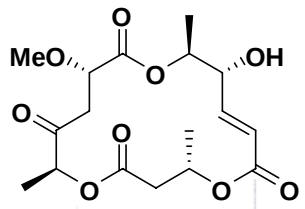



**18**

**$^1$H-NMR ($CDCl_3$, 300 MHz)**

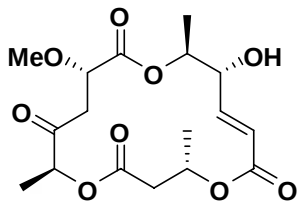





**1**

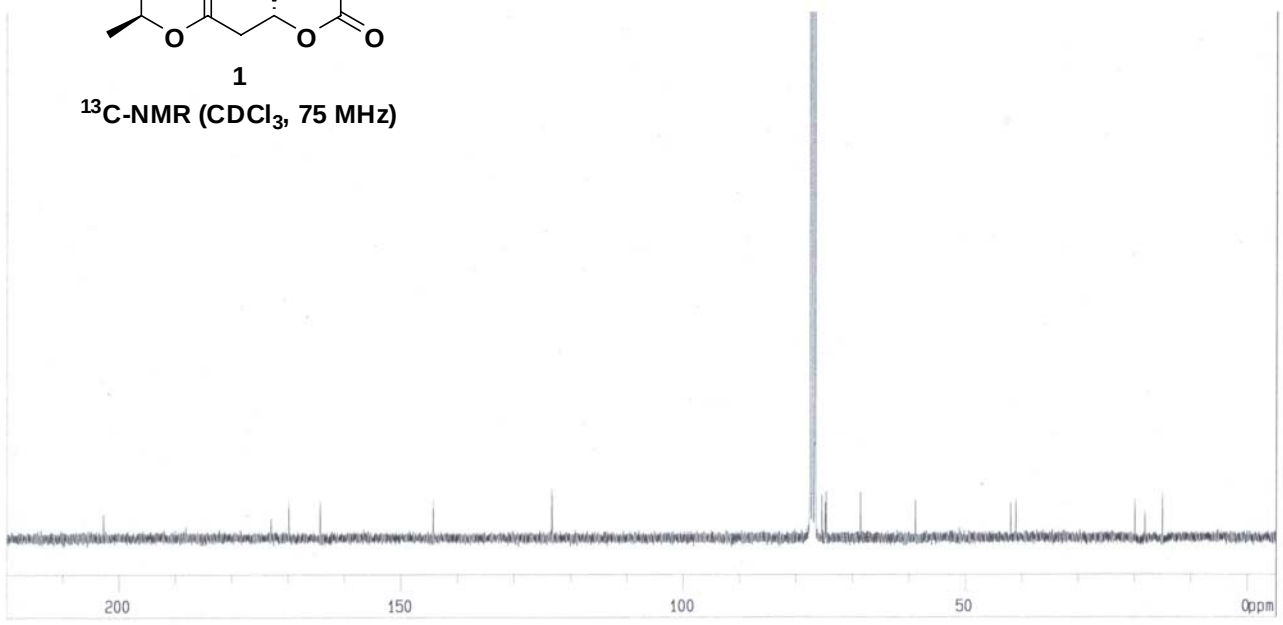
**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**

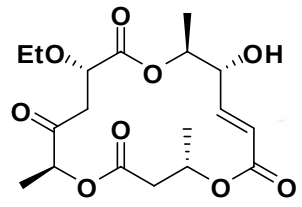



**1**

**$^{13}$C-NMR ($CDCl_3$, 75 MHz)**

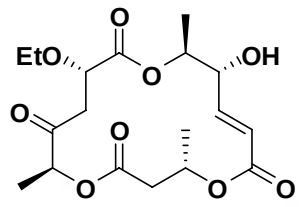





**2**

**$^{1}$H-NMR ($CDCl_3$, 300 MHz)**




**2**

**$^{13}$C-NMR ($CDCl_3$, 75 MHz)**